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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,396	11/28/2000	James F. Young	10271-007-999	8214

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EXAMINER	
BROWN, STACY S	

ART UNIT	PAPER NUMBER
1648	13

DATE MAILED: 03/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,396	YOUNG ET AL.	
	Examin r	Art Unit	
	Stacy S Brown	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *February 13, 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-199* is/are pending in the application.

4a) Of the above claim(s) *192* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-191 and 193-199* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 November 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election of Group I, claims 1-72 and 85-199 is acknowledged. The restriction requirement between Groups I and II is withdrawn. In response to Applicant's traversal of the restriction requirement, the restriction requirement with regard to the selection of one antibody and one amino acid sequence for claims 18, 44, 72, 139, 179 and 192 is withdrawn. Instead, a species election is required for claims 18, 44, 72, 139, 179 and 192. Applicants elected SYNAGIS™ and SEQ ID NO: 3.

2. Claims 1-191 and 193-199 are examined on the merits. Claim 192 does not recite SYNAGIS™ and will not be examined in this Office Action.

Specification

3. The abstract of the disclosure is objected to because the last sentence lacks a period. Correction is required. See MPEP § 608.01(b).

Claim Objections

4. Claims 45-46 and 198 are objected to because of the following informalities:

Claims 45-46 contain a minor grammatical error in the phrase "after the administration said first dose".

Claim 198 has two periods at the end of claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18, 44-72, 77, 78, 77, 78, 81, 82, 85-122, 139, 140-161, 168-179 and 193-199 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 83, 84, 140-148, 156-161, 168-179 recite "increased" half-lives which lacks comparative basis. It is not clear to what standard "increased" is being measured and compared. Clarification is required.

Claims 18, 44, 72, 77, 78, 81, 82, 85-122, 139, 149-155, 170 and 193-199 contain the trademark/trade name SYNAGIS™ or HL SYNAGIS™. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe an antibody and, accordingly, the identification/description is indefinite.

Claims 45-72, 85-110 and 140-158 are indefinite because it is not clear what is meant by "therapeutically effective" and "prophylactically effective". The claims should define endpoints that indicate effectiveness has been achieved, such as is indicated in claim 19 which recites a specific serum titer that is maintained.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-9, 14-17, 74, 76 and 80 are rejected under 35 U.S.C. 102(b) as being anticipated by Brams *et al.* (U.S. Patent 5,811,524). The claims are drawn to methods of preventing, treating and/or ameliorating RSV infection and associated symptoms in a human, particularly an infant. The methods comprise the administration of one or more antibodies that immunospecifically bind to one or more RSV antigens. The antibodies can be human monoclonals or humanized monoclonals and are administered in an amount less than 15 mg/kg and have an affinity of at least $1 \times 10^8 M^{-1}$ or $2 \times 10^8 M^{-1}$.

Brams discloses methods for treating and preventing RSV infection in human newborn infants comprising the administration of human monoclonal antibodies that have an affinity for RSV F-protein of $2 \times 10^9 M^{-1}$ or $1 \times 10^{10} M^{-1}$. Brams' antibodies are administered in a variety of ways: intravenous, intramuscular, intraperitoneal or aerosol. The dosage of antibodies is preferably 100 to 5000 μg/kg, see column 20, lines 13-43. Therefore, the Brams reference anticipates claims 1-9 and 14-17.

7. Claims 1, 5-6, 9 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Johnson *et al.* (cited in IDS, reference CD). The claims are summarized above. Johnson

discloses a humanized monoclonal antibody (MEDI-493) that prevents RSV infection. The method comprises the administration of a humanized monoclonal antibody that recognizes a conserved neutralizing epitope on the F protein, see abstract. The antibodies are administered to high-risk infants intravenously in the amount of 2.5 mg/kg, see abstract. Therefore, Johnson *et al.* anticipate claims 1, 5-6, 9 and 14.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-72 and 85-199 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brams et al. (U.S. Patent 5,811,524) or Johnson *et al.* (cited in IDS, reference CD) in view of MedImmune (package insert for SYNAGIS™ last revised December 2, 1999), Johnson (cited in IDS, reference AF) and Lam *et al.* (cited in IDS, reference CG).

Claims 1-18 are generally drawn to methods of preventing, treating and/or ameliorating RSV infection and associated symptoms in a human, particularly an infant. The methods comprise the administration of one or more antibodies that immunospecifically bind to one or more RSV antigens. The antibodies can be human monoclonals or humanized monoclonals and are administered in an amount less than 15 mg/kg and have an affinity of at least 1 X 10^8 M^{-1} or 2 X 10^8 M^{-1}. The antibodies are administered 1-5 times during RSV season. Claims 19-44 are drawn to methods similar to claim 1, wherein the effective serum titer of antibodies is less than

30μg/ml at least 20 days after administration and prior to the administration of a subsequent dose. Claims 45-72 are drawn to methods similar to claim 1, wherein the effective serum titer of antibodies is maintained for at least 20 days after the administration of a first dose and prior to the administration of a subsequent dose. Claims 73-139 are drawn to a pharmaceutical composition and methods (similar to claim 1) of preventing, treating and/or ameliorating RSV infection. The composition can be sustained release type. Claims 140-148 are drawn to methods similar to claim 1 wherein the antibodies administered have increased *in vivo* half-lives. Claims 149-155 are drawn to methods similar to claim 1 wherein one of the antibodies administered is SYNAGIS™. Claims 156-179 are drawn to methods similar to claim 1 wherein antibody concentration in the patient is less than 30 μg/ml at least 30 days after the administration of a first dose and prior to the administration of a subsequent dose. Claim 179 is limited to SEQ ID NO: 3 which encodes a VH CDR3. Claims 180-199 are drawn to methods similar to claim 1 wherein a prophylactic dosage results in a concentration of at least 20 ng of antibodies per 1 mg of lung protein at least 20 days after the administration of a first dose and prior to the administration of a subsequent dose.

The teachings of Brams and Johnson (reference CD) are summarized above. Brams and Johnson do not teach the administration of SYNAGIS™ in combination with other antibodies 1-5 times during RSV season, nor do they teach a sustained release pharmaceutical composition, nor do they disclose increased *in vivo* half-lives.

MedImmune's package insert for SYNAGIS™ discloses increased half-lives of an *average* 20 days administered to pediatric patients less than two years old. The concentrations of antibodies achieved with intramuscular injections of 15 mg/kg resulted in concentrations of 37

+/- 21 μg/ml (16 to 58 μg/ml) after the first injection, see column 1, "Clinical Pharmacology". The dosage recommended is 15 mg/kg of body weight, on a monthly basis during RSV season (November through April).

Johnson *et al.* (reference AF) discloses human-murine chimeric antibodies against RSV. In Johnson's methods of treating and preventing RSV, monoclonal antibodies can be administered as part of a plurality of human antibodies against RSV F epitopes, not necessarily binding to the same epitopes of the F protein, see column 4, lines 41-46.

Lam *et al.* (reference CG) disclose sustained release microencapsulation pharmaceutical formulations of recombinant humanized monoclonal antibodies for patients with macular degeneration, see abstract.

It would have been *prima facie* obvious to incorporate MedImmune's antibody into the formulation of Brams or Johnson (CD). One would have been motivated by Johnson (AF) who discloses that a plurality of human antibodies against RSV F epitopes can be administered as a treatment or prophylactic composition for RSV. One would have had a reasonable expectation of success that the incorporation of MedImmune's antibody could have been administered in a combination treatment with the antibodies of Brams or Johnson, which bind to F epitopes of RSV. Johnson (AF) shows that it was well known in the art to combine antibodies for treatment.

It would have been *prima facie* obvious to modify the treatments of Brams or Johnson (CD) by packaging them in a sustained release vehicle as taught by Lam *et al.* One would have been motivated because Lam provides sustained release microencapsulations for humanized monoclonal antibodies. Lam shows that sustained release vehicles for antibody delivery is well known and well practiced in the art of pharmacy. One would have had a reasonable expectation

of success that the sustained release formulation of Lam would also work with the antibodies taught by Brams, Johnson (CD), and the combination of Brams, Johnson (CD), MedImmune and Johnson (AF) because Lam's formulation is specific for humanized monoclonal antibodies, and the antibodies of the above cited references are human/humanized monoclonal antibodies.

Regarding the limitation in claim 179, which is limited to SEQ ID NO: 3 which encodes a VH CDR3, the Office does not give patentable weight to the sequence because it does not appear to make any contribution over the prior art's antibodies. Applicant is invited to point out any special characteristics that SEQ ID NO: 3 provides to the antibody.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

It is noted that the asserted novelty of the invention is that the antibodies of the instant invention are superior to the prior art's antibodies because increased half-life, antibody/antigen binding affinity and dosage. However, all the limitations of the instant claims are encompassed by the prior art. Applicant is invited to specify any contributions over the antibodies disclosed in the prior art.

Conclusion

9. No claim is allowed.

Papers relating to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 located in Crystal Mall 1. The Fax number for Art Unit 1648 is (703) 308-4426. All Group 1600 Fax machines will be available to receive transmissions 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Stacy S. Brown, whose telephone number is (703) 308-2361. The Examiner can normally be reached on Monday through Friday and alternate Wednesdays from 6:30 AM-4:00 PM, (EST). If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, James C. Housel, can be reached at (703) 308-4027. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Stacy S. Brown
March 22, 2002

HANKYEL T. PARK, PH.D
PRIMARY EXAMINER